An Efficient Gene Editing System to Tag and Isolate HIV-Infected Cells

Brief Description of Technology
Highly specific tagging and sorting of latently infected cells, facilitating cell expansion for subsequent genetic and phenotypic studies.

Technology Overview
HIV can persist in a latent state for decades within human immune cells despite life-sustaining advances in modern anti-retroviral therapy (ART). Current standard of care treatment reduces viral loads and improves outcomes of those living with HIV, but has no effect on latently infected cells which provide a life-long reservoir of infectious virions. These latently infected cells pose the greatest challenge to curing HIV, but account for as little as 0.003% of peripheral blood cells. To overcome the challenge posed by the scarcity of these cells in patients, genetic engineers at Fred Hutch have developed a method for tag-and-target isolation of latently infected cells. Dr. Jerome and his team use CRISPR/Cas9-based homology-independent target insertion (HITI) together with a reporter lacking a polyA signal to label HIV provirus in viable immune cells, and virtually eliminate off-target background noise. This breakthrough paves the way for vital research of latent viral infection and sets the stage for curative therapeutic development.

Applications
- Analysis of provirus integration dynamics, T cell preference, and viral reactivation mechanics
- Targeting and isolation of non-HIV proviruses [e.g., HTLV and HERVs]
- Tagging of rare blood cells with off-target noise reduction

Advantages
- Unmasks low abundance cells from blood [e.g., circulating tumor cells]
- HITI requires no sequence homology for genetic editing which overcomes the difficulty of sequence variability inherent to HIV

Market Overview
The global HIV drug market was valued at $25.3 billion in 2018 and is expected to grow to $40.7 billion by 2026 giving a CAGR of 6.1%. ART is currently the major market driver for HIV/AIDS treatment. While ART reduces disease burden and improves patient outcomes, a curative treatment targeting latent infection is still an unmet need for the nearly 40 million patients living with HIV.